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Attention: International Preliminary Examining Authority

Our Ref: **P21647WO/PWC/DM/KS**
Your Ref:

14 May 2001

COPY

Dear Sirs

International (PCT) Patent Application No. PCT/GB00/00908
In the name of Oxford GlycoSciences (UK) Ltd

I write in response to the Official Communication of 29th December 2000. Please find enclosed an amended set of claims in triplicate to replace those currently on file.

Claims 1 to 3 have been amended to only include those protein features that have not been previously described as markers for breast cancer in the prior art. The features removed are namely cytokeratin 18, cytokeratin 8, fructose bisphosphate aldolase, cytokeratin 14, cathepsin D, HSP 27 and HSP 94. The protein feature thioredoxin peroxidase 2 has not been removed as this is completely different from the protein thioredoxin disclosed in document D1. Therefore, all the features included in claims 1 to 3 have not previously been disclosed as markers for breast cancer, and so this should overcome the lack of unity objection.

Claims 1 to 3 have also been amended to cover methods comprising the step of identifying one or more differentially present protein features in a biological sample. This amendment should clarify the matter for which protection is sought.

The protein features excised from claims 1 to 3 have been included in the new claim 4.

In addition original claims 18 to 20 have been moved so that they now follow new claim 9, so they are grouped together with the claims on which they are dependent.

I look forward to receiving your comments in light of these amendments.

Yours faithfully

CHAPMAN, Paul William
Agent for the Applicants

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CLAIMS

1. A method for screening-and or diagnosis of breast cancer in a human subject, which comprises the step of identifying one or more differentially present protein features in a biological sample obtained from said human subject, wherein the protein features are any one or more of: BF-1, BF-3, BF-4, BF-5, BF-6, BF-7, BF-8, BF-9, BF-10, BF-11, BF-12, BF-13, BF-14, BF-15, BF-16, BF-17, BF-18, BF-19, BF-20, BF-21, BF-23, BF-24, BF-25, BF-28, BF-29, BF-31, BF-33, BF-35, BF-36, BF-37, BF-38, BF-39, BF-40, BF-41, BF-43, BF-46, BF-47, BF-48, BF-49, BF-50, BPI-1, BPI-3, BPI-4, BPI-5, BPI-6, BPI-7, BPI-8, BPI-9, BPI-10, BPI-11, BPI-12, BPI-13, BPI-14, BPI-15, BPI-16, BPI-17, BPI-18, BPI-19, BPI-20, BPI-21, BPI-23, BPI-24, BPI-25, BPI-28, BPI-29, BPI-31, BPI-33, BPI-35, BPI-36, BPI-37, BPI-38, BPI-39, BPI-40, BPI-41, BPI-43, BPI-46, BPI-47, BPI-48, BPI-49, or BPI-50.

2. A method for monitoring and/or assessing breast cancer treatment in a human subject, which comprises the step of identifying one or more differentially present protein features in a biological sample obtained from said human subject, wherein the protein features are any one or more of: BF-1, BF-3, BF-4, BF-5, BF-6, BF-7, BF-8, BF-9, BF-10, BF-11, BF-12, BF-13, BF-14, BF-15, BF-16, BF-17, BF-18, BF-19, BF-20, BF-21, BF-23, BF-24, BF-25, BF-28, BF-29, BF-31, BF-33, BF-35, BF-36, BF-37, BF-38, BF-39, BF-40, BF-41, BF-43, BF-46, BF-47, BF-48, BF-49, BF-50, BPI-1, BPI-3, BPI-4, BPI-5, BPI-6, BPI-7, BPI-8, BPI-9, BPI-10, BPI-11, BPI-12, BPI-13, BPI-14, BPI-15, BPI-16, BPI-17, BPI-18, BPI-19, BPI-20, BPI-21, BPI-23, BPI-24, BPI-25, BPI-28, BPI-29, BPI-31, BPI-33, BPI-35, BPI-36, BPI-37, BPI-38, BPI-39, BPI-40, BPI-41, BPI-43, BPI-46, BPI-47, BPI-48, BPI-49, or BPI-50.

3. A method for identifying the presence or absence of metastatic breast cancer in a human subject, which comprises the step of identifying one or more differentially present protein features in a biological sample obtained from said human subject, wherein the protein features are any one or more of: BF-1,

BF-3, BF-4, BF-5, BF-6, BF-7, BF-8, BF-9, BF-10, BF-11, BF-12, BF-13, BF-14, BF-15, BF-16, BF-17, BF-18, BF-19, BF-20, BF-21, BF-23, BF-24, BF-25, BF-28, BF-29, BF-31, BF-33, BF-35, BF-36, BF-37, BF-38, BF-39, BF-40, BF-41, BF-43, BF-46, BF-47, BF-48, BF-49, BF-50, BPI-1, BPI-3, BPI-4, BPI-5, BPI-6, BPI-7, BPI-8, BPI-9, BPI-10, BPI-11, BPI-12, BPI-13, BPI-14, BPI-15, BPI-16, BPI-17, BPI-18, BPI-19, BPI-20, BPI-21, BPI-23, BPI-24, BPI-25, BPI-28, BPI-29, BPI-31, BPI-33, BPI-35, BPI-36, BPI-37, BPI-38, BPI-39, BPI-40, BPI-41, BPI-43, BPI-46, BPI-47, BPI-48, BPI-49, or BPI-50.

4. A method as claimed in any one of claims 1 to 3 further comprising identifying one or more protein features selected from: BF-2, BF-22, BF-26, BF-27, BF-30, BF-32, BF-42, BF-44, BF-45, BF-51, BPI-2, BPI-22, BPI-26, BPI-27, BPI-30, BPI-32, BPI-42, BPI-44, BPI-45, and BPI-51.

5. A method as claimed in any one of claims 1 to 4 wherein the biological sample is a serum sample or a tissue sample.

6. A method as claimed in any one of claims 1 to 6 wherein a "cluster" or subset of the totality of protein features defined in tables I, II, III and IV is identified.

7. A method as claimed in any one of claims 1 to 6 wherein the method comprises an immunoassay step utilising one or more antibodies against one or more of the protein features defined in tables I, II, III and IV, or a derivative, homologue or fragment thereof.

8. A method as claimed in claim 7 wherein the immunoassay is a competitive immunoassay, a non-competitive assay system using techniques such as western blots, a radioimmunoassay, an ELISA (enzyme linked immunosorbent assay), a "sandwich" immunoassay, an immunoprecipitation assay, a precipitin reaction, a gel diffusion precipitin reaction, an immunodiffusion assay, an agglutination assay, a complement-fixation assay, an immunoradiometric

assay, a fluorescent immunoassay , a protein A immunoassay, ab Immunoprecipitation assay or an Immunohistochemical assay.

9. A method as claimed in any one of claims 1 to 6 wherein the method comprises the use of nucleic acid probes and/or PCR reactions to amplify nucleic acid coding for one or more of the protein features defined in tables I, II, III and IV.

10. A method as claimed in any one of claims 1 to 6 wherein a whole body or organ scan of the subject is carried out to determine localisation of breast tissue cells, particularly metastatic breast cancer cells.

11. A method as claimed in claim 19 wherein labelled antibodies are employed.

12. A method as claimed in claim 20 wherein the antibodies are radiolabelled.

13. An antibody which specifically binds to a protein feature as defined in tables I, II, III or IV.

14. An antibody as claimed in claim 13 which is for use in the screening for and/or diagnosis of breast cancer in a human subject.

15. An antibody as claimed in claim 13 or claim 14 which is a monoclonal antibody.

16. An antibody as claimed in any one of claims 13 to 15 wherein the antibody is adapted/modified such that binding to the protein will be localised to the site of the breast cancer cells, preferably metastatic breast cancer cells.

17. A diagnostic kit comprising one or more reagents for use in the detection and/or determination of one or more of the protein features defined in tables I, II, III and IV.

18. A kit as claimed in claim 17 which comprises one or more containers with one or more antibodies against one or more of the protein features.

19. A kit as claimed in claim 18 which further comprises a labeled binding partner to the antibody and/or a solid phase (such as a reagent strip) upon which the antibody(ies) is/are immobilized.

20. A kit as claimed in claim 17 which comprises a nucleic acid probe capable of hybridizing to DNA or RNA encoding one or more of the protein features defined in Tables I, II, III or IV.

21. A kit as claimed in claim 20 which comprises in one or more containers a pair of primers (*e.g.*, each in the size range of 6-30 nucleotides, more preferably 10-20 nucleotides) that are capable of priming amplification under appropriate reaction conditions of at least a portion of a nucleic acid encoding a protein feature as defined in Tables I, II, III or IV.

22. A method for the treatment of breast cancer, particularly metastatic breast cancer, which comprises administering to a subject suffering from said breast cancer, an effective amount of one or more antibodies against one or more of the protein features defined in Tables I, II, III or IV, in association with or conjugated to an agent capable of causing cell death.

23. A method as claimed in claim 22 wherein the agent is a cytotoxic agent or a cytostatic agent.

24. The use of one or more antibodies against one or more of the protein features defined in Tables I, II, III or IV, in association with or conjugated to an agent capable of causing cell death in the manufacture of a medicament for the treatment of breast cancer, particularly metastatic breast cancer.